

## REMARKS

Claims 1-3 and 6-15 are pending. Claims 1, 6, 7, and 9-15 are under consideration. All claims under consideration stand rejected under 35 U.S.C. § 103(a).

The Office Action asserts that claims 1, 6, 9-12, 14, and 15 are unpatentable over Ho *et al.* (WO 00/56711) in view of Torigoe *et al.* (U.S. 6,600,022). Applicants respectfully disagree. In light of Ho *et al.* and Torigoe *et al.*, at the time of filing, one of skill in the art would not have had a reasonable expectation that an antibody that binds the IL-18 receptor component of SEQ ID NO:4 would be successful in treating the indicated diseases.

As summarized in Applicants' specification (Background; pp. 1-2), there was uncertainty by those of skill in the art whether blocking IL-18 *in vivo* would lead to a beneficial or deleterious effect (*citing* Dayer, 1999, *J. Clin. Invest.* 104:1337-1339). IL-18 likely played a variety of roles *in vivo* including negatively regulating the maturation of pro-inflammatory cytokines such as IL-1 $\beta$  and itself. Given the pleiotrophic and contradictory roles played by IL-18, Dayer warned that one should not conclude that blocking IL-18 would help in treating, for example, rheumatoid arthritis. Ho *et al.* merely reports that the monoclonal antibodies to IL-18 neutralize the effect of IL-18 on PBMCs *in vitro* (Example 2 and Table I). Torigoe *et al.* reports that the monoclonal antibody to IL-18R inhibited IL-18-induced IFN- $\gamma$  production in KG-1 cells *in vitro* (Example 3-2(c)). Neither Ho *et al.* nor Torigoe *et al.* quell the speculation regarding the *in vivo* effects of blocking IL-18. Thus, at the time of filing, one of skill in the art could not reasonably conclude that blocking IL-18 *in vivo* by targeting the IL-18 receptor would have efficacy in treating a medical disorder selected from the group consisting of psoriasis, renal failure due to ischemia, and viral hepatitis.

The Office Action further asserts that claim 7 is unpatentable over Ho *et al.* (WO 00/56711) in view of Torigoe *et al.* (U.S. 6,600,022) and Huston *et al.* (Proc. Natl. Acad. Sci., 1988, 85(16):5879-83). As stated above, Ho *et al.* and Torigoe *et al.* would not provide one of skill in the art with a reasonable expectation that an antibody that binds the IL-18 receptor component of SEQ ID NO:4 would be successful in treating the indicated diseases. Huston *et al.* relates to single chain antibodies and fails to overcome the deficiencies of the other cited references.

The Office Action also asserts that claim 13 is unpatentable over Ho *et al.* (WO 00/56711) in view of Torigoe *et al.* (U.S. 6,600,022) and Jacobs *et al.* (U.S. 5,605,690). As stated above, Ho *et al.* and Torigoe *et al.* would not provide one of skill in the art with a reasonable expectation that an antibody that binds the IL-18 receptor component of SEQ ID NO:4 would be successful in treating the indicated

diseases. Jacobs et al. relates to a TNF antagonist and fails to overcome the deficiencies of the other cited references.

Applicants' disclosure removes the speculation held by those of skill in the art as to the effect of blocking IL-18 to treat inflammatory diseases. The specification demonstrates *in vivo* efficacy of treating several different inflammatory diseases with compounds that block IL-18 (See Examples; pp. 24-32). As acknowledged in the Office Action, the present claims are enabled by the specification. Thus, the present claims are nonobvious and enabled.

In light of the above remarks, Applicants respectfully request withdrawal of the rejections of the claims. If further discussion would help expedite allowance of the claims, the Examiner is welcomed to contact the undersigned at the telephone number provided.

Respectfully submitted,



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I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below.

Signed: Shanti M. Kersten Date: Feb. 10, 2006  
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